

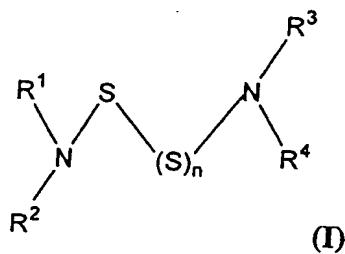
Appl. No. 09/763,616
Amendment dated: June 22, 2005
Reply to OA of: October 20, 2004

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

Claims 1-41(canceled).

43(new) A method of treating a disease condition caused or exacerbated by an HPV wherein said disease condition is cervical cancer or precursor lesions thereof, asymptomatic infections of the cervix and genital, common, plantar or planar warts, comprising the administration to a mammal in need thereof of an effective amount of a compound which facilitates disruption of a chelated metal cation domain of a protein encoded for by an HPV gene, wherein the compound is selected from the group of compounds consisting of formulae (I):



wherein

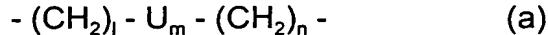
n is selected from 1-5

R¹ - R⁴ are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted acyl, optionally substituted heterocyclil, halo alkyl, arylalkyl, carboxy, carboxy ester and carboxamido; or

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R¹ and R² together, and/or R³ and R⁴ together, independently form a group of formula (a):



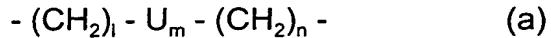
wherein: U is CH₂, O, NH or S;

l and n are independently selected from 0 to 6 and m is 0 or 1 when U is CH₂ and m is 1 when U is O, NH or S, such that

l + m + n is greater than or equal to 2;

and wherein any one or more (CH₂) or NH groups may be further optionally substituted or a pharmaceutically acceptable derivative thereof.

44(new). A method according to claim 43 wherein R¹ and R² together, and/or R³ and R⁴ together, independently form a group of formula (a):



wherein: U is selected from CH₂, O, NH or S;

l and n are independently selected from 0 to 6 and m is 0 or 1 when U is CH₂ and m is 1 when U is O, NH or S, such that

l + m + n is greater than or equal to 2;

and wherein any one or more (CH₂) or NH groups may be further optionally substituted.

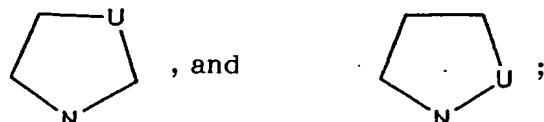
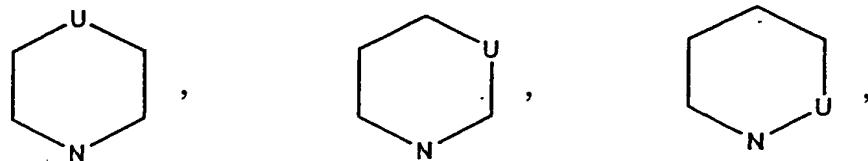
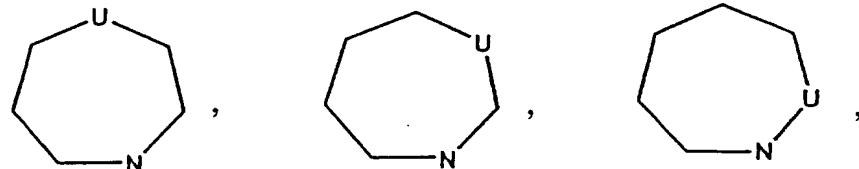
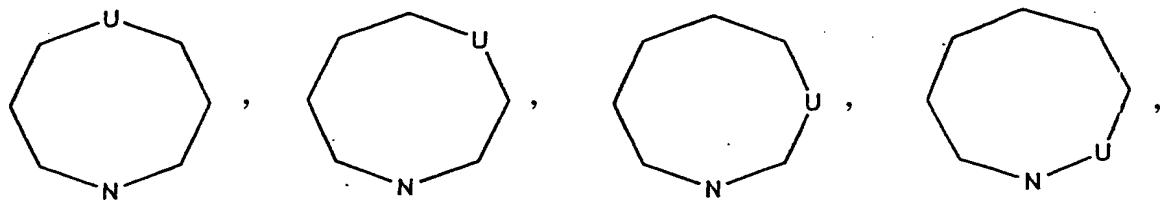
45(new). A method according to claim 44 wherein U is CH₂.

46(new). A method according to claim 45 wherein formula (a) is selected from the group consisting of - (CH₂)₂-, -(CH₂)₃-, -(CH₂)₄-, -(CH₂)₅-, -(CH₂)₆- and -(CH₂)₇-.

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47(new). A method according to claim 44 wherein U is NH, O, or S and m is 1.

48(new). A method according to claim 44 wherein R₁ and R₂, and/or R₃ and R₄, together with the nitrogen to which they are attached independently form a group selected from the group consisting of:



which may be optionally substituted at a carbon atom, and/or where U is NH, at the nitrogen atom.

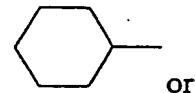
49(new). A method according to claim 48 wherein R₁ and R₂, and/or R₃ and R₄, together with the nitrogen to which they are attached each independently form an optionally substituted morpholino, thiomorpholino, or piperazino group.

50(new). A method according to claim 44 wherein any -CH₂- group of formula (a) is optionally substituted by one or more of the groups selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, hydroxy, halo, methoxy, ethoxy, iso-propoxy, acetoxy, optionally substituted benzyl, optionally substituted pyridyl, optionally substituted pyrimidyl and optionally substituted phenyl.

51(new). A method according to claim 43 wherein at least one of R¹ - R⁴ is independently selected from the group consisting of: hydrogen, optionally substituted phenyl, optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted cyclopentyl, and optionally substituted cyclohexyl, formyl, acetyl.

52(new). A method according to claim 50 wherein the optional substituent is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, hydroxy, halo, methoxy, ethoxy, iso-propoxy, acetoxy, and phenyl.

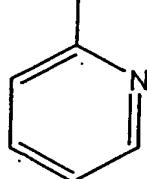
53(new). A method according to claim 43 wherein at least one of R¹-R⁴ is selected from the group consisting of:

-CH₂-Ph, -CH₂-C(O)-O-CH₂CH₃, -C(O)H, -CH₂-CH₃ and  or

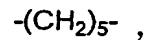
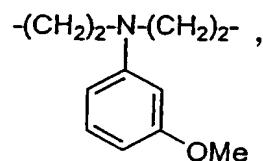
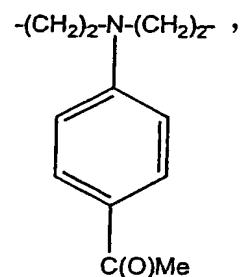
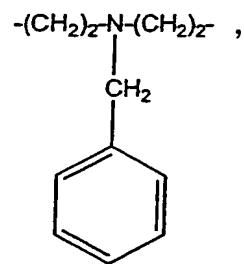
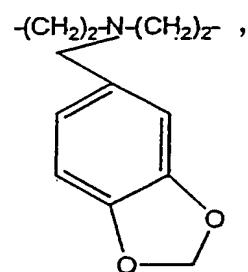
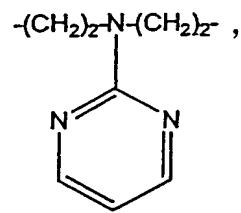
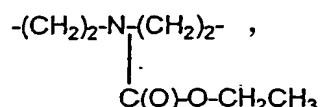
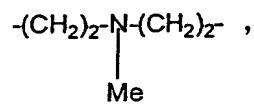
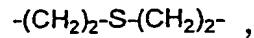
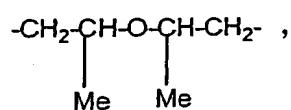
R¹ and R² together and/or R³ and R⁴ together independently form a group selected from the group consisting of:

- $(CH_2)_2-O-(CH_2)_2-$, - $(CH_2)_5-$,

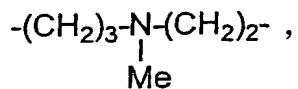
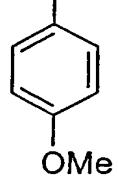
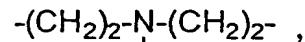
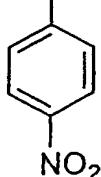
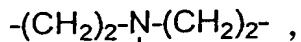
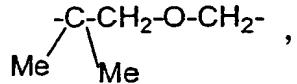
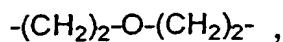
- $(CH_2)_2-N-(CH_2)_2-$, - $(CH_2)_3-$,



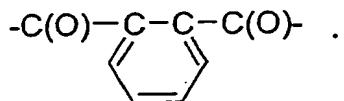
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$-(\text{CH}_2)_2^-$, and



54(new). A method according to claim 43 wherein n is 1, 2 or 3.

55(new). A method according to claim 43 wherein the HPV is HPV-16.

56(new). A method according to claim 55 wherein the protein is the HPV-16 E6 or E7 oncoprotein.

57(new). A method according to claim 43 wherein the HPV is HPV-18.

58(new). A method according to claim 57 wherein the protein is the HPV-18 E6 or E7 oncoprotein.

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59(new). A method according to claim 43 where the chelated metal cation domain is a chelated zinc cation domain.

60(new). A method according to claim 59 wherein the chelated zinc domain is the sequence motif cys-X2-cys-X29-cys-X2-cys (SEQ ID NO:2).

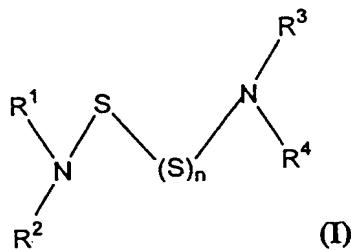
61(new). A method of treating a disease condition caused or exacerbated by an HPV which is cervical cancer or precursor lesions thereof, asymptomatic infections of the cervix and genital, common, plantar or planar warts comprising the administration of an effective amount of a compound as defined in claim 43 to a mammal in need thereof.

62(new). A method according to claim 43 wherein the compound is capable of effecting at least 30% zinc release in a TSQ assay and/or inhibits or reduces the binding of an E6 protein to E6AP or E6BP and/or exhibits selective cytotoxicity towards MPV-infected cells.

63(new). A method according to claim 43 wherein the disease or condition is cervical cancer or its HPV associated precursor lesions.

64(new). A method of treating a disease condition caused or exacerbated by an HPV and which is cervical cancer or precursor lesions thereof, asymptomatic infections of the cervix and genital, common, plantar or planar warts comprising the administration of an effective amount of a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an HPV gene to a mammal in need thereof, wherein said compound is a compound identified as a compound useful in the treatment of a disease or condition caused or exacerbated by an HPV by a method which comprises contacting a protein molecule containing a chelated metal cation domain, encoded by an HPV gene, with an effective amount of

said compound for a time and under conditions sufficient to facilitate disruption of the chelated metal cation domain and directly or indirectly determining the amount of chelated metal cation released wherein the amount of chelated metal cation released is indicative of the disruption of the chelated metal cation domain wherein the compound is selected from the group of compounds consisting of formulae (I):

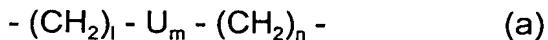


wherein

n is selected from 1-5

R^1 - R^4 are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted acyl, optionally substituted heterocyclyl, halo alkyl, arylalkyl, carboxy, carboxy ester and carboxamido; or

R^1 and R^2 together, and/or R^3 and R^4 together, independently form a group of formula (a):



wherein: U is CH_2 , O , NH or S ;

l and n are independently selected from 0 to 6 and m is 0 or 1 when U is

CH_2 and m is 1 when U is O , NH or S , such that

$l + m + n$ is greater than or equal to 2;

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and wherein any one or more (CH₂) or NH groups may be further optionally substituted or a pharmaceutically acceptable derivative thereof.

65(new). The method according to claim 43 wherein the compound is 4,4-dithiodimorpholine.

66(new). A method according to claim 43 wherein n is 1 or 2.